Environmental Tobacco Smoke and Sudden Infant Death Syndrome: A Review

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Background

Environmental tobacco smoke (ETS), containing the developmental neurotoxicant, nicotine, is a prevalent component of indoor air pollution. Given that there is a strong association with active maternal smoking and sudden infant death syndrome (SIDS), this project aimed to ascertain whether SIDS may also be associated with ETS exposure in infants of nonsmoking mothers.

Is there an association?

Table 1. Studies examining paternal/household smoking and risk of SIDS outcomes: variations in study design and outcome

Reference	n case	n cont.	Surveyed time of smoking	Surveyed location of smoking	Surveyed amount of smoking	Analyzed effect among nonsmoking mothers?	Odds ratio (95% CI); Adjusted for maternal smoking during pregnancy and other factors	
							Paternal	Household
Nicholl & O'Cathain, 1992	242	251	unspecified	unspecified	cigarettes/day	Yes	-	-
Schonedorf & Keily, 1992	435	6098	Postnatal	unspecified	Unspecified	Yes	-	1.41[w] (1.04, 1.90) 0.93[aa] (0.68, 1.27)
Mitchell et al., 1993	485	1800	Postnatal	unspecified	cigarettes/day	Yes	1.37 (1.02, 1.84)	1.17 (0.84, 1.63)
Klonoff-Cohen et al., 1995	200	200	Prenatal Postnatal	Around mother; room w/ infant	# adults smoking; cigarettes/day	No	- 3.46[a] (1.91, 6.28)	- 2.18[a] (1.09, 4.38)
Blair et al., 1996	195	780	unspecified	Around infant	cigarettes/day	Yes	2.50 (1.48, 4.22)	-
Brooke et al., 1997	147	276	unspecified	unspecified	# parents smoking; cigarettes/day	Yes	-	-
Alm et al., 1998	244	869	Before preg. Prenatal Postnatal	unspecified	# adults smoking; cigarettes/day	Yes	0.8[B] (0.5, 1.2) 0.9[p] (0.6, 1.4) 1.2[a] (0.8, 1.9)	- - 1.2[a] (0.6, 2.2)
Dwyer et al., 1999	35	9000	Prenatal Postnatal	Around mother; room w/ infant	# adults smoking; cigarettes/day	No	-	0.72 (0.48, 1.46)
Carpenter et al., 2004	745	2411	Postnatal	unspecified	cigarettes/day	No	- -	1.07[1] (0.71, 1.61) 1.54[2] (1.11, 2.14)

[B]Paternal smoking before pregnancy; [p]Paternal/ other smoking during pregnancy; [a]Paternal/ other smoking after birth; [w] White infants; [aa] African American infants; [1]1 – 9 cigarettes/day; [2]10 – 19 cigarettes/day

Review Results: There are few epidemiologic studies that examine paternal and household smoking. Among these studies, the following limitations are present:

- **Paternal/household smoking exposures are most often *only* measured in the postnatal period, and not prenatally**
- **Exposure data is vague; specific information regarding the amount or location of smoking is not known in many instances**
- **Only 6 out of 9 studies examined the risk of SIDS in paternal smoking/maternal nonsmoking environments (Table 2)**
- **Small sample size is an issue in several studies, particularly in the sub-analyses**
- **Odds ratios (given in Tables 1 & 2) are inconsistent across studies**

Table 2. Paternal-only smoking sub-analyses

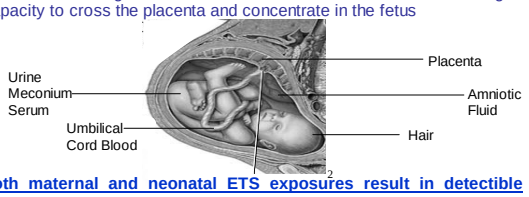
Reference	Sub-analysis				Odds Ratio (95% CI); Paternal smoker & maternal nonsmoker*
	ETS exposure (non-maternal)		No exposure		
	Cases	Controls	Cases	Controls	
Nicholl & O'Cathain, 1992	52	67	54	97	1.39 1.63 (1.11, 2.40)**
Schonedorf & Keily, 1992	not provided	not provided	not provided	not provided	1.33 (0.77, 2.27)[w] 1.00(0.62, 1.58)[aa]
Mitchell et al., 1993	not provided	not provided	not provided	not provided	1.00(0.64-1.56)
Blair et al., 1996	40	163	33	421	3.41 (1.98, 5.88)
Brooke et al., 1997	11	45	20	137	1.72 (0.94, 3.13) 2.12 (0.99, 4.55)***
Alm et al., 1998	18	138	74	462	0.8 (0.5, 1.5)[a]

* All ORs are unadjusted unless otherwise noted
** Adjusted for birth weight, maternal age, gravidity, and housing repair
*** Adjusted for maternal age, maternal marital status, maternal education, sleep position, co-sleeping, type of bedclothes, mattress type, birth weight, and previous illness; [a] Postnatal exposures only; [w] White infants; [aa] African American infants

Therefore, it is unclear if a strong association exists between paternal or household smoking and SIDS, but some association is suggested. Present information indicates a need for further exploration regarding the biologic plausibility such a relationship.

Biologic Plausibility

1. **Nicotine readily crosses the placenta** Nicotine specific biomarkers are detected in fetal/neonate tissues and fluids (see below), often in concentrations higher than those found in maternal fluids indicating a capacity to cross the placenta and concentrate in the fetus



[2]

2. **Both maternal and neonatal ETS exposures result in detectible nicotine/cotinine in biological samples** Nicotine specific biomarkers are found at measurable levels in infants of nonsmoking mothers exposed to ETS. Concentrations are significantly higher than in unexposed infants and similar to levels found in infants of light active maternal smokers
3. **Nicotine is a potent developmental neurotoxicant** Nicotine displays the capacity to impair arousal and awakening responses in hypoxic environments (following table)

Study	Species	Dose of nicotine	Expos. period	Measure	Outcome
Lewis and Bosque, 1995	Human Infant; 8-12 weeks	Maternal Smoking	Pre/ post natal	Observation of awakening response, or its absence	?54% of infants of smokers failed to awaken ?15% of infants of nonsmokers failed to awaken
Slotkin et al., 1995	Rat	0, 2, 6 mg/kg/ day	Prenatal	Mortality	Significantly higher mortality at highest dose
Fewell and Smith, 1998	Rat	0, 6 mg/kg/ day	GD5 – PD 5-6	?Time to last gasp ?Autoresus.	?No effect in time to last gasp ?Exposed sustained significantly fewer periods of hypoxia
Campbell et al., 2001	Infant	Maternal Smoking	Active maternal smoking	Ventilatory responses	Increased ventilatory sensitivity observed in exposed; exposed more likely to wake from asphyxia
Fewell and Smith, 2001	Rat	0, 1.5, 3, 6 mg/kg/ day	GD 6 – PD 5-6	?Time to last gasp ?Autoresus.	?No effect in Time to last gasp ?Rats exposed at 3 and 6 mg/kg/day sustained significantly fewer periods of hypoxia than lower exposures and controls
Hafstrom, 2002	Lamb	0, 0.5 mg/kg/ day	Last 49 days of gest.	Time to arousal from sleep during hypoxia	Time significantly longer in exposed

4. **Nicotinic acetylcholine receptor (nAChR) binding may provide a mechanistic basis for developmental toxicity** Nicotine binding to nAChRs may induce excessive and/or premature release of neurotransmitters, possibly leading to altered development of the nervous system (Slotkin, 2004), or inhibition of arousal mechanisms (Hafstrom et al., 2002).

Conclusions

- Relatively few investigative efforts have explored the association between SIDS and perinatal ETS exposure.
- Despite inconsistencies in existing epidemiologic evidence, non-maternal smoking does appear to have some effect on an infant's risk of SIDS.
- Such an association is biologically plausible given the detection of nicotine and cotinine in fetal and neonatal tissues and fluids in infants of nonsmoking mothers.
- Acting on nAChRs, nicotine is capable of disrupting a developing nervous system in such a way that normal mechanisms for responding to hypoxia are inhibited.
- While impaired recovery from hypoxia is seen most clearly in animal studies at high doses of nicotine, it is observed at doses near or equal to ETS exposures.
- Efforts should be made not only to discourage pregnant women from actively smoking, but also to discourage fathers and household member from smoking around pregnant mothers and neonates.

[2]http://www.nlm.nih.gov/medlineplus/ency/images/ency/fullsize/17010.jpg

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